

# Introduction to Diffusion-weighted Imaging

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National Institutes of Health

# Motivation

- Magnetic resonance imaging provides information about the spatial distribution of water.
- Diffusion-weighted MRI (DWI) provides information about the motion of water.
- DWIs are sensitive to cellular architecture and tissue integrity.
- DWI can provide quantitative measures that are directly comparable.
- Diffusion imaging can be used to identify specific white matter tracts
- ~570 publications combining fMRI and DWI

# Outline

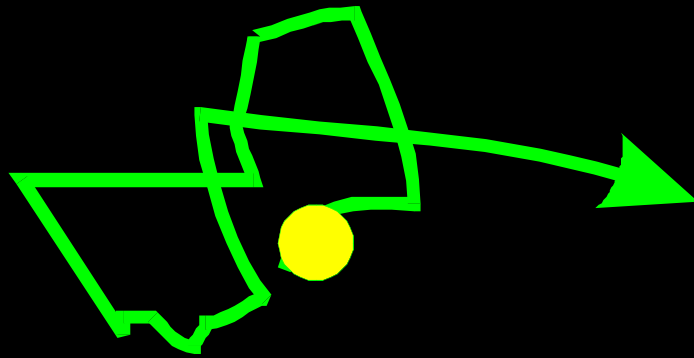
- What is diffusion?
- How do we measure diffusion in MRI?
- How do we extract directional information?
- What are the practical problems and limitations?
- Beyond the diffusion tensor

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# Diffusion

- Diffusion refers to the random translational (Brownian) motion of molecules that results from the thermal energy of these molecules

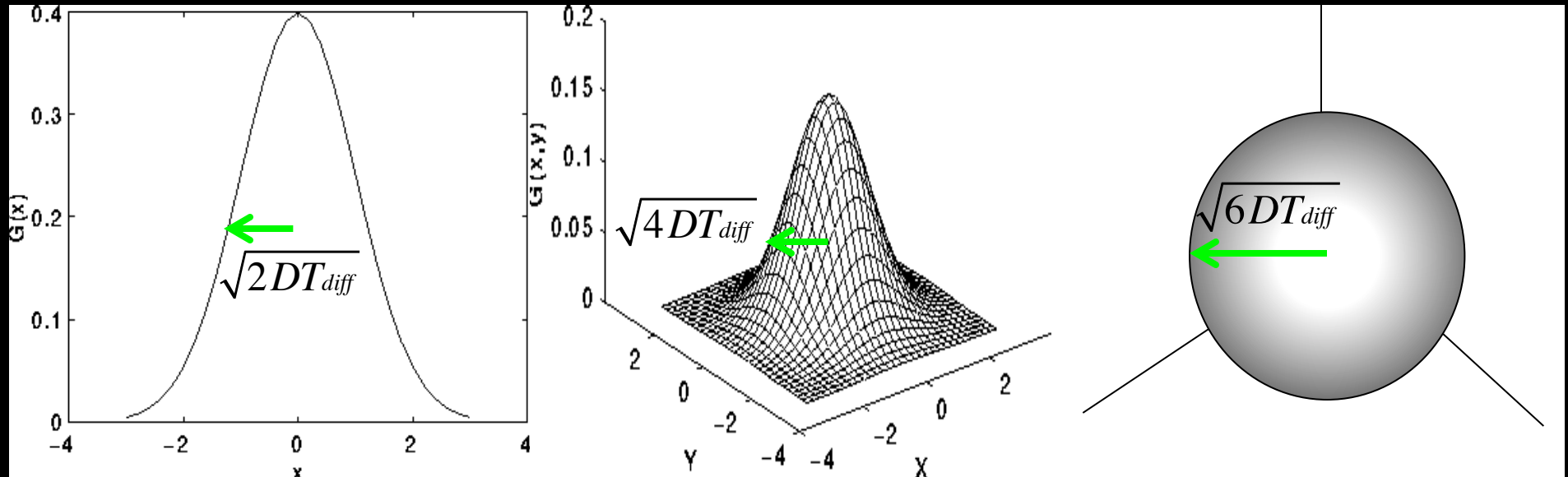


$$D = \frac{kT}{6\pi\eta R_H} \quad (\text{for sphere})$$

Stokes-Einstein

# Gaussian Distribution

- Large number of particles that are free to diffuse have a squared displacement of a Gaussian form



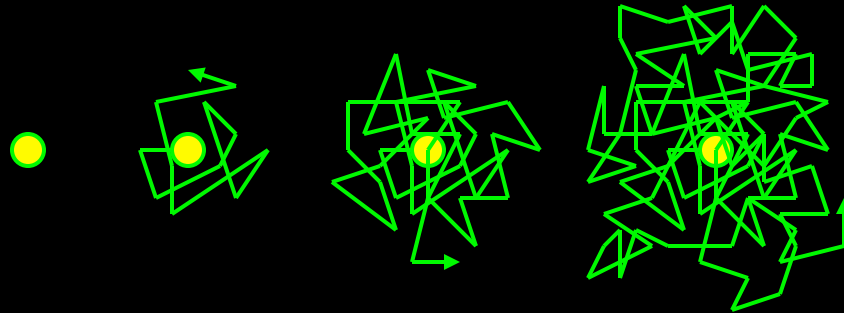
1D

2D

3D

Einstein, A. Ann Physik (1905) 4: 549-590

# Diffusion



$$\langle r^2 \rangle \approx 6DT_{dif}$$

For  $\text{H}_2\text{O}$  at  $37^\circ \text{C}$

$$D \approx 3.0 \times 10^{-3} \text{ mm}^2/\text{s}$$

$$T_{dif} \approx 30 \text{ ms}$$

$$r \approx 25 \text{ } \mu\text{m}$$

- If the motion of water is hindered by cell membranes, macromolecules, etc. the displacement will be less and  $D$  will appear lower.

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# Image Intensity in MRI

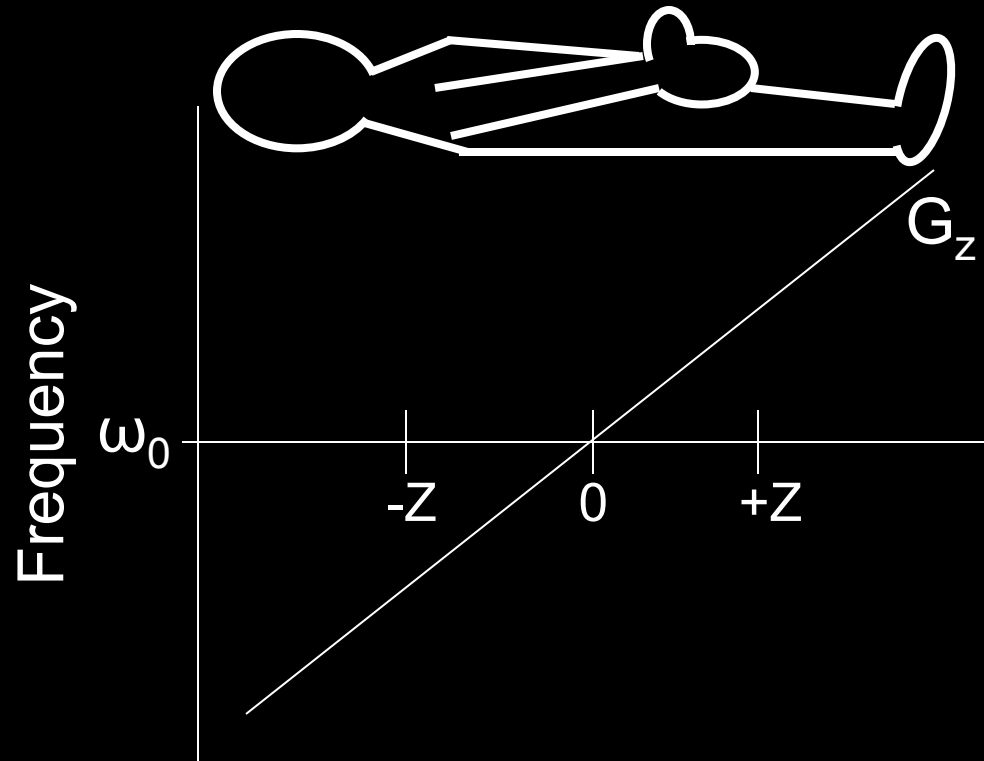
- Physical property of tissue water

– $\rho$	proton density	Concentration of water
– T1	relaxation time	} Rotational motion, Magnetic field strength
– T2	relaxation time	
– T2*	relaxation time	
– D	diffusion coefficient	Translational motion

- Experimentally controlled parameters

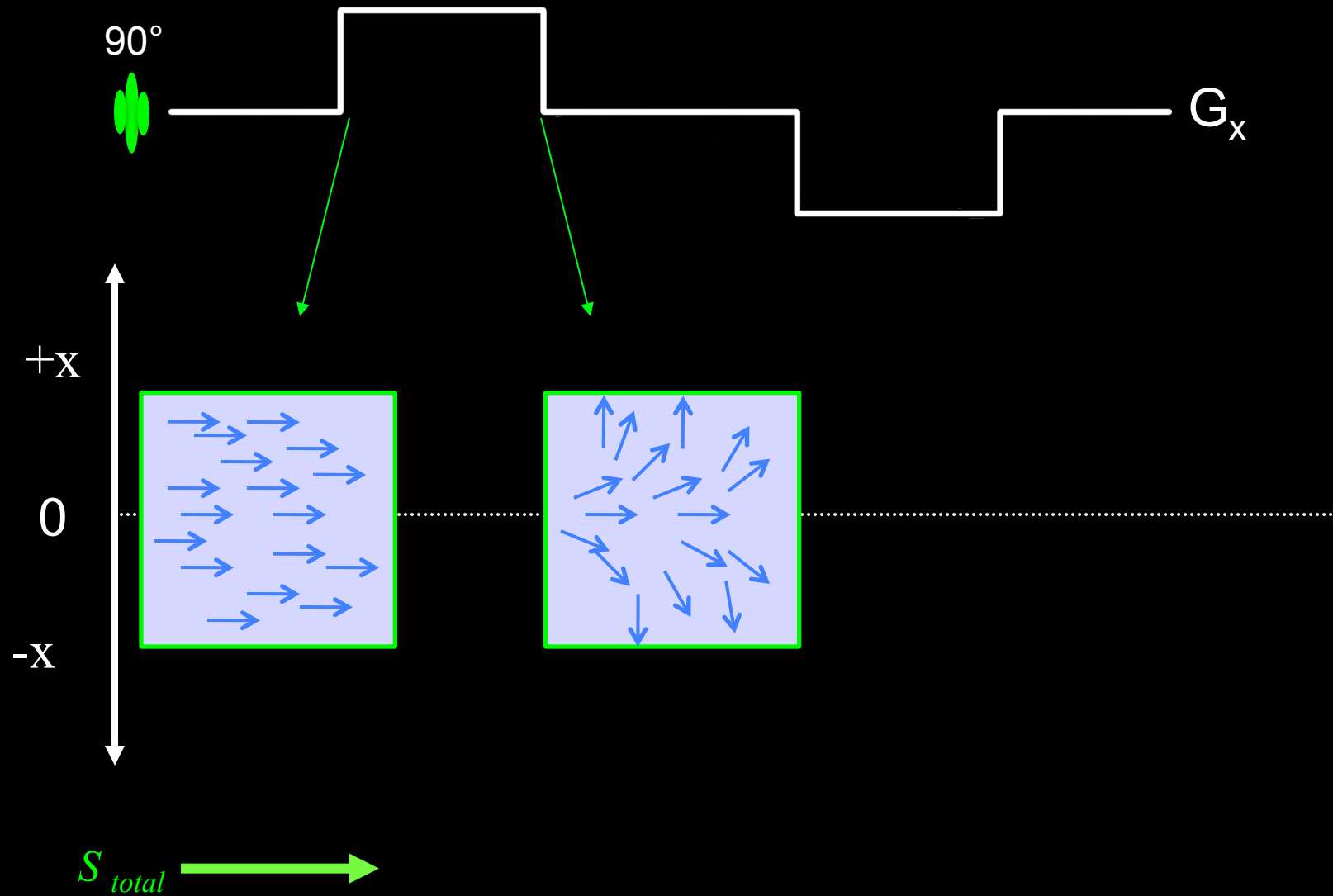
– Sequence	Spin-echo/gradient echo
– TR	Time of Repetition
– TE	Time to echo
– b-value	diffusion-weighting factor

Gradients make the resonance frequency a function of spatial position



$$\omega = \gamma B = \gamma B_0 + \gamma z G_z$$

# Basic Diffusion-weighting

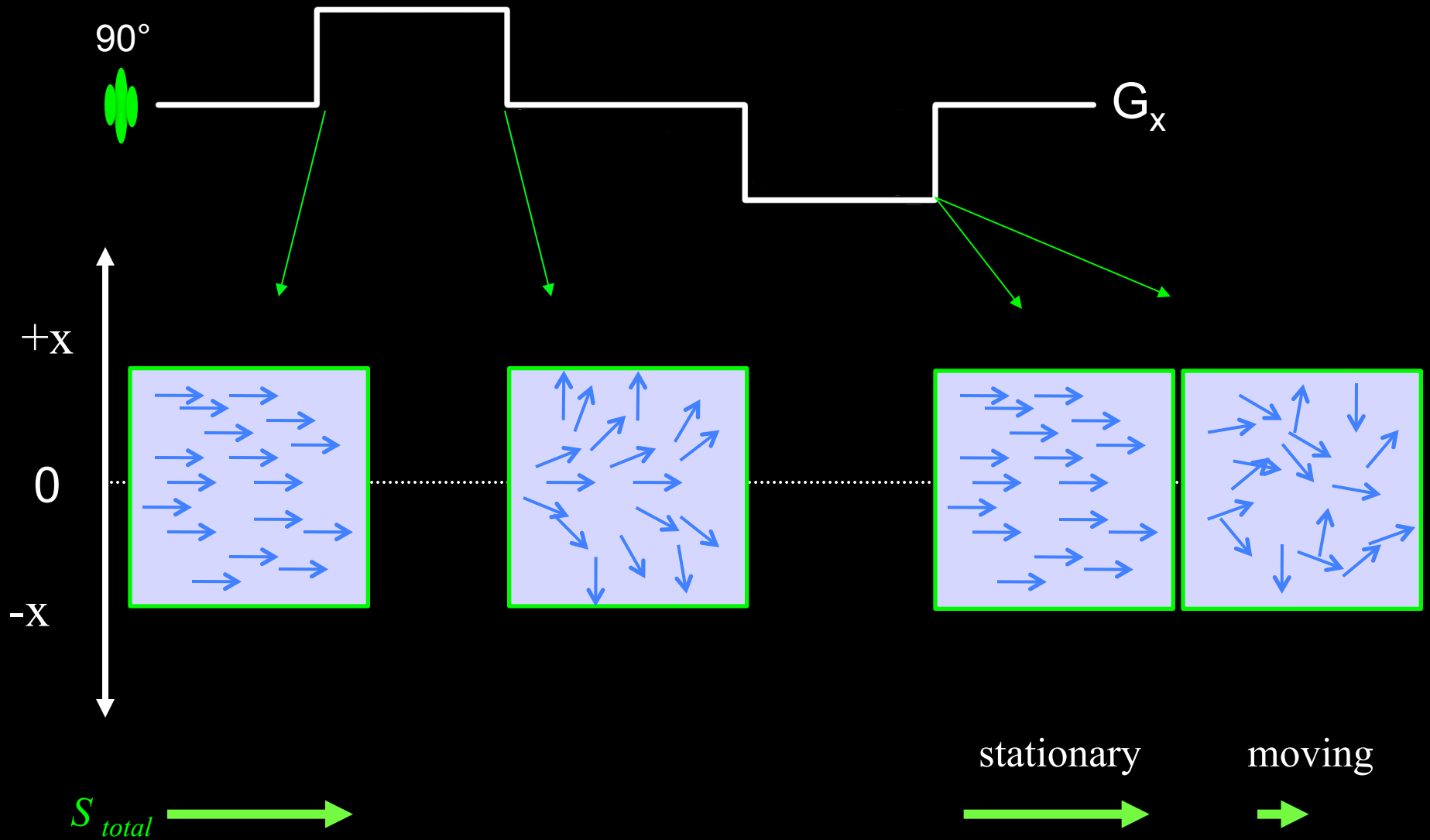


# Phase Twist

-x  
0  
+x

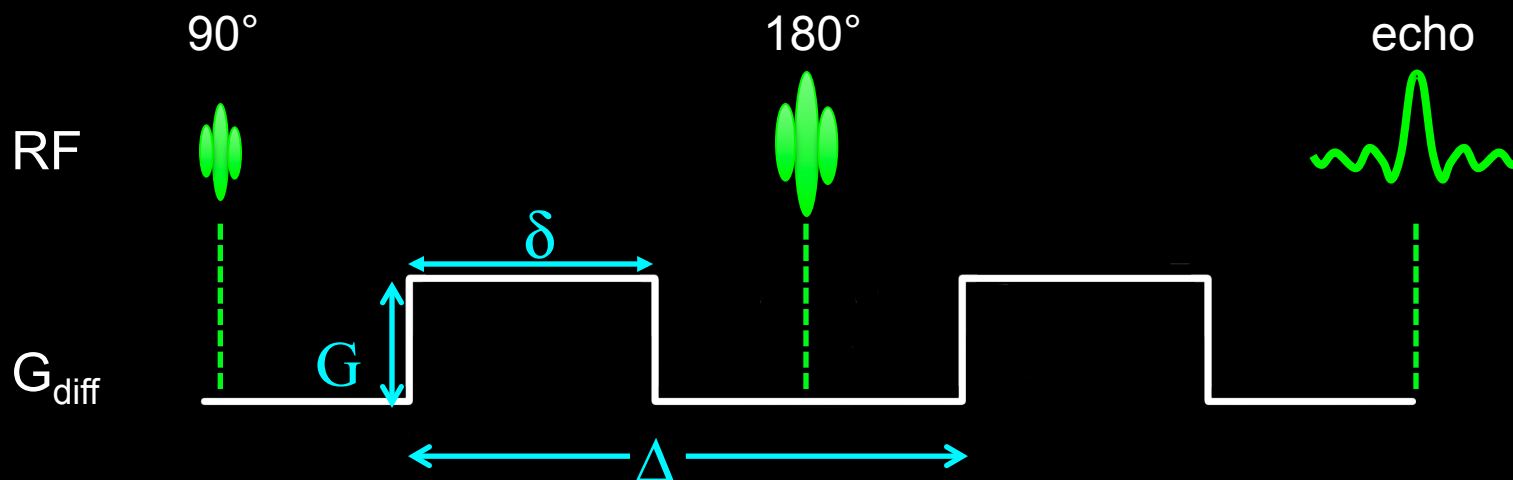


# Basic Diffusion-weighting



Short Break for a Video

# Spin-echo Diffusion Preparation



$$b = (\gamma G \delta)^2 \left( \Delta - \frac{\delta}{3} \right)$$

Stejskal, EO and Tanner, JE. J Chem Phys (1965) 42 : 288-292

# DWI

$$S = S_0 e^{-bD}$$

Non-diffusion-weighted  
signal intensity

B-value  
sec/mm<sup>2</sup>

Diffusion  
Coefficient  
mm<sup>2</sup>/sec

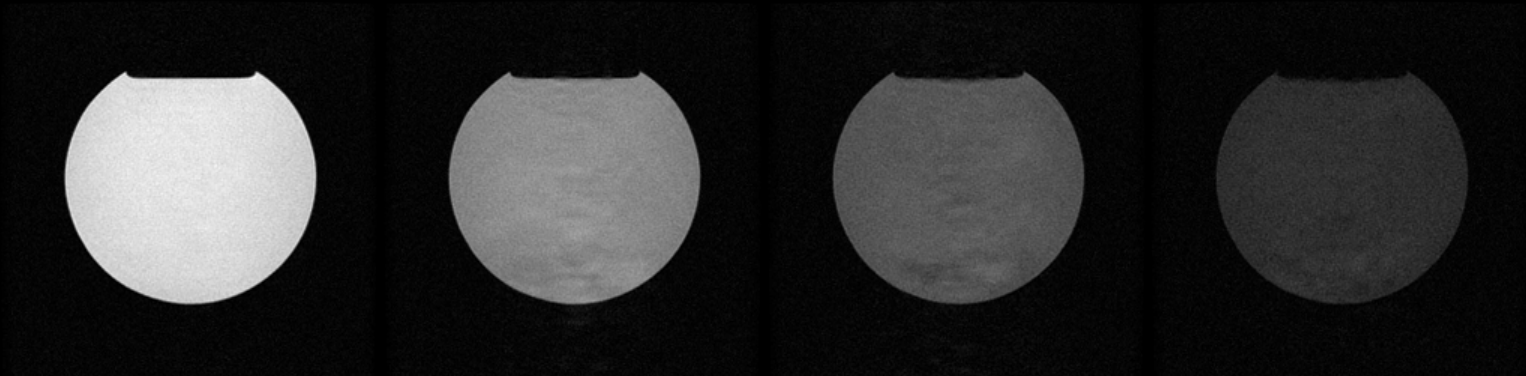
# Typical DWI

- Single-shot “spin-echo” Echo Planar Imaging

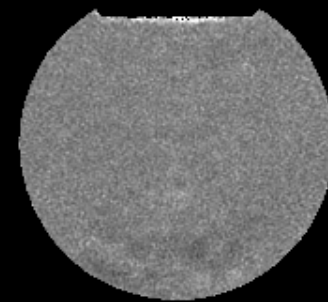
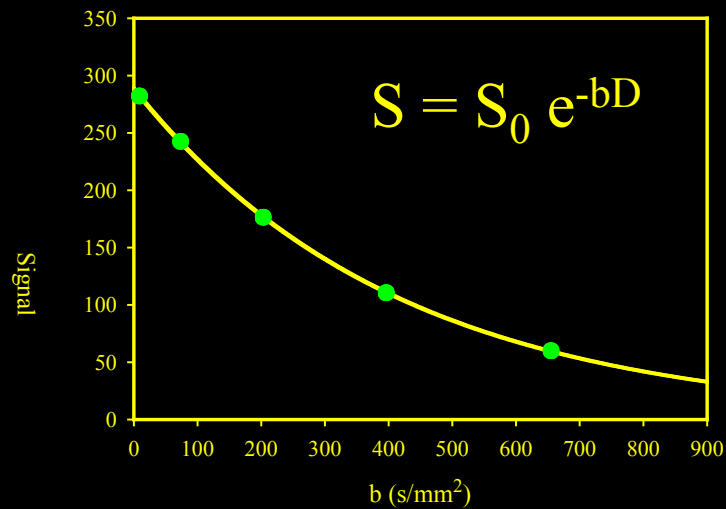
Parameter	Value	Comment
TE	50-100ms	Limited by b-value
TR	>5s	Fully relaxed
Matrix	96 x 96	2.5 x 2.5 mm
Slice Thickness	2.5 mm	Equal dimensions
B-value	~1000 s/mm <sup>2</sup>	For brain*

\*Jones D., *et al.* Mag Res Med (1999) 42 : 515

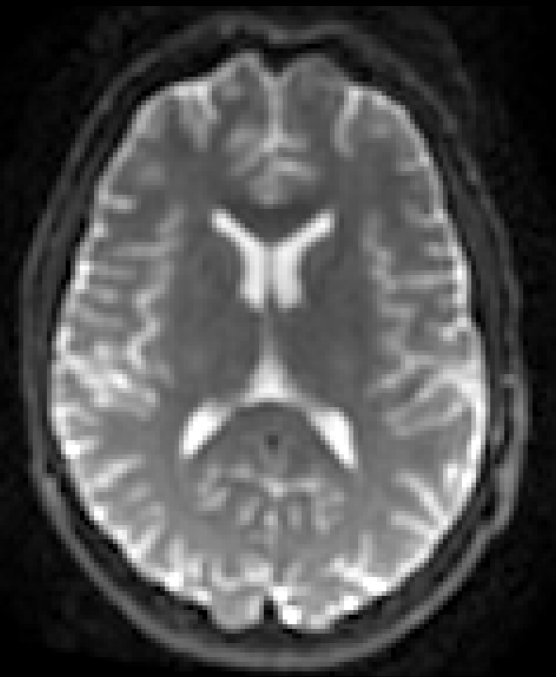
# Calculate Diffusion Parameters



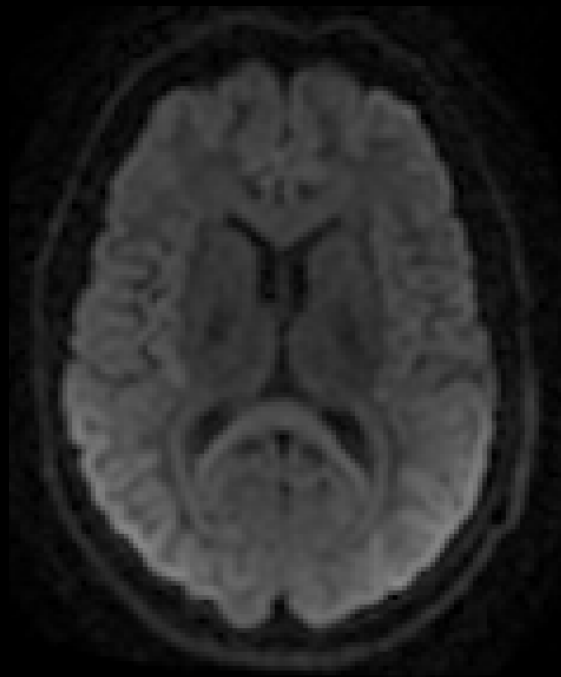
$b$  (s/mm<sup>2</sup>)      8                      200                      400                      650



Diffusion map



$b = 0 \text{ s/mm}^2$   
 $I_0$



$b = 1100 \text{ s/mm}^2$   
 $I_z$

$$I_z = I_0 e^{-bD_z}$$



$D_z$

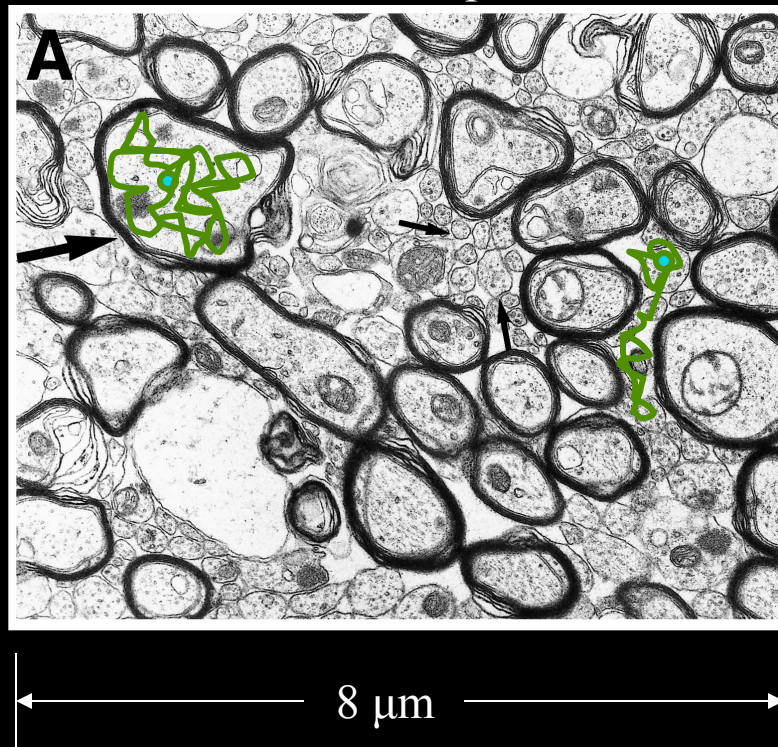
$$D_z = \frac{1}{-b} \ln \left( \frac{I_z}{I_0} \right)$$

# Water Diffusion in Tissue

## Not Free

Cell membranes  
Organelles  
Extracellular matrix

EM of mouse corpus callosum



## Anisotropy

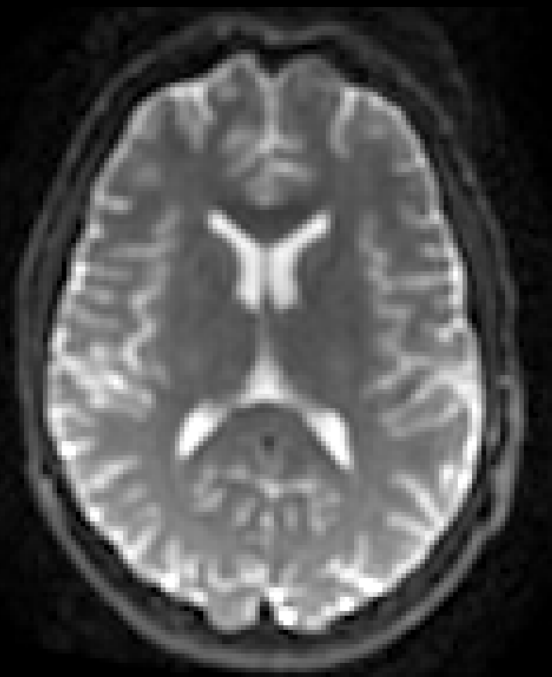
$D_{\text{perpendicular}}$



$D_{\text{parallel}}$



$D_{\text{perp}} \ll D_{\text{par}}$

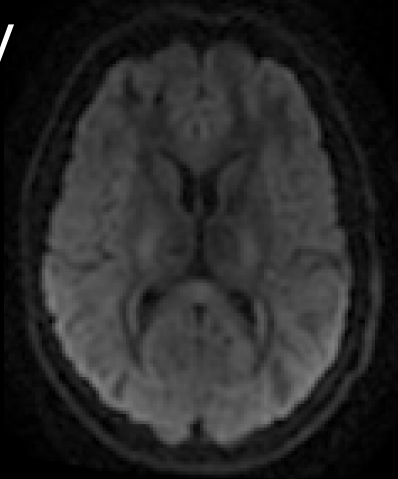
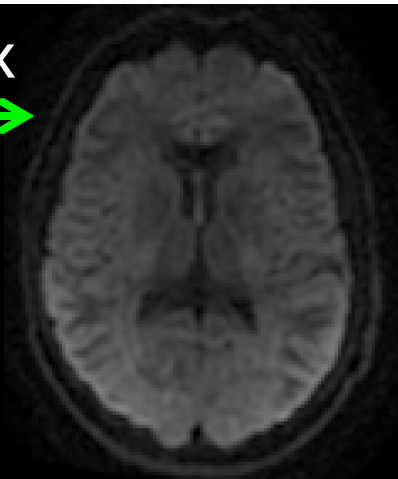


$b = 0 \text{ s/mm}^2$

Gx  
↔

Gy  
↕

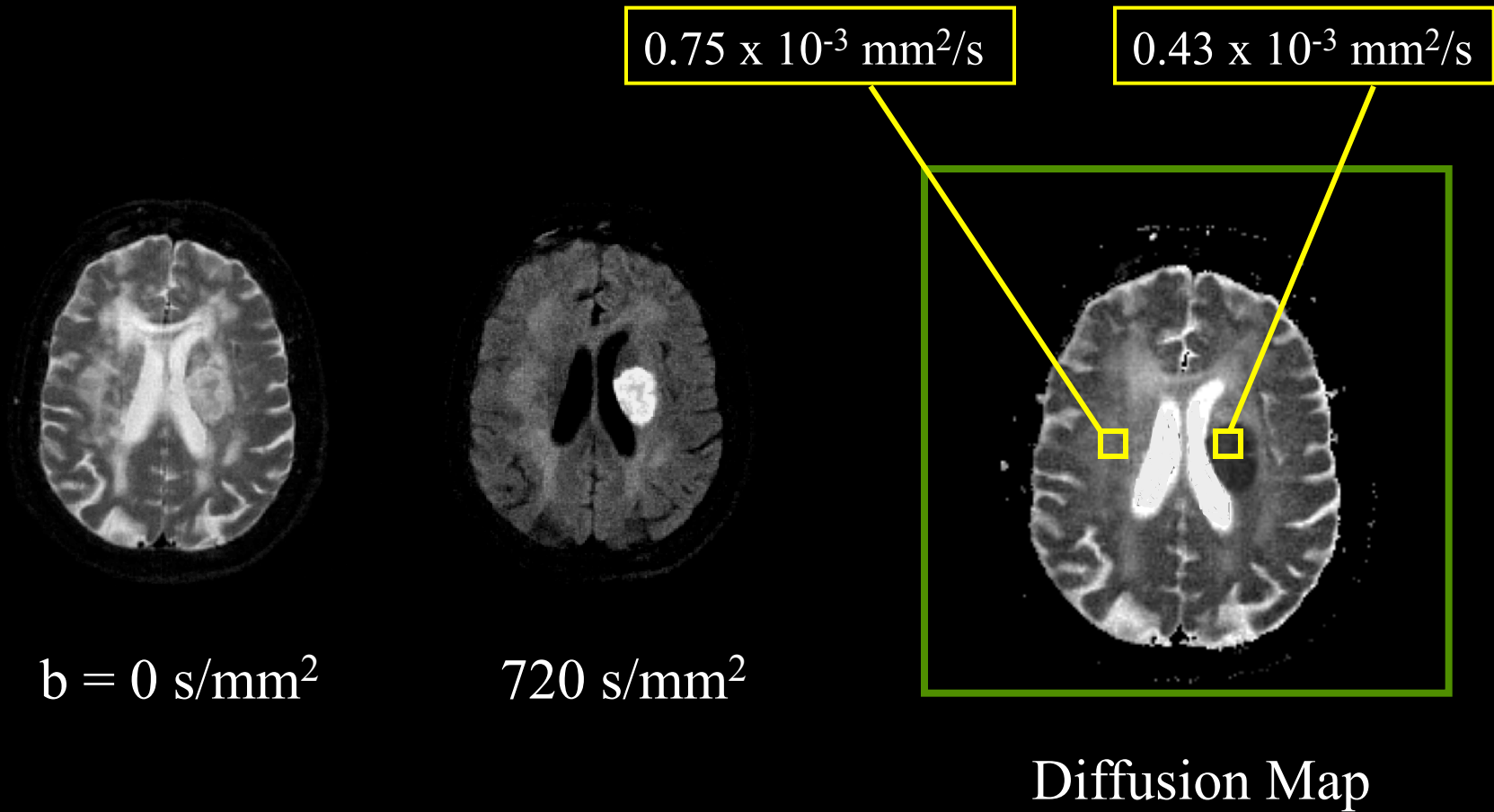
Gz  
⊗



ADC

$$ADC = \frac{1}{-b} \ln \left( \frac{I_{ave}}{I_0} \right)$$

# Acute Stroke



Warach S., et al. Ann Neurol (1995) 37:231-241

# Outline

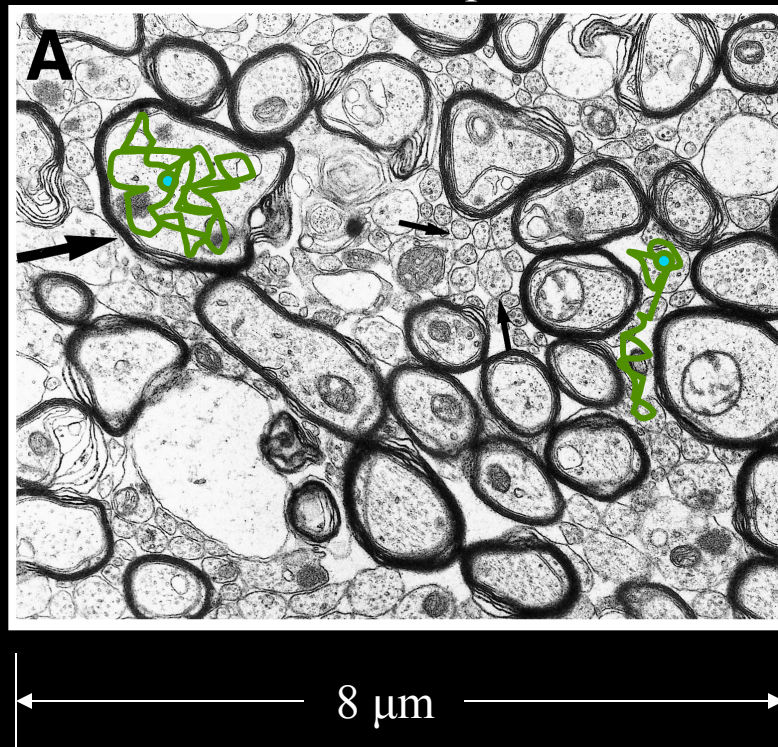
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# Water Diffusion in Tissue

## Not Free

Cell membranes  
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EM of mouse corpus callosum



## Anisotropy

$D_{\text{perpendicular}}$

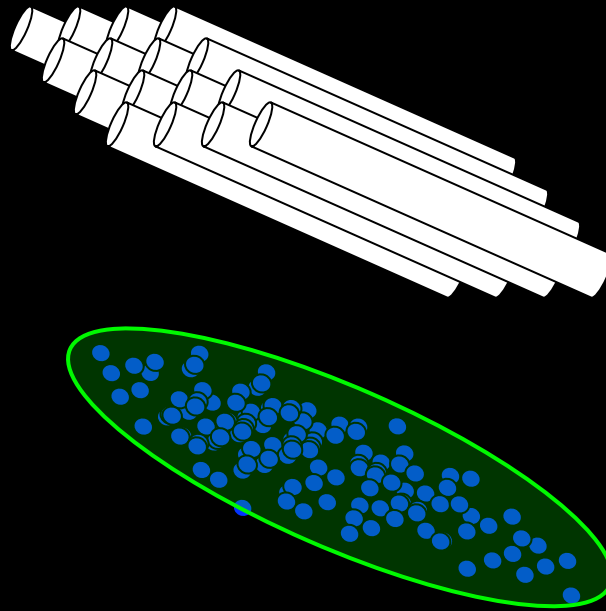


$D_{\text{parallel}}$

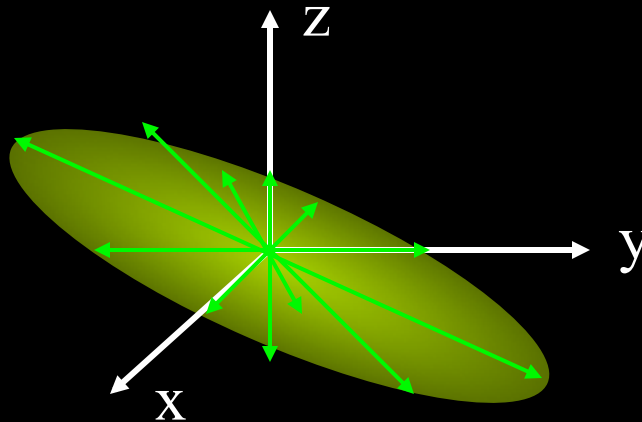


$D_{\text{perp}} \ll D_{\text{par}}$

# Anisotropic Diffusion



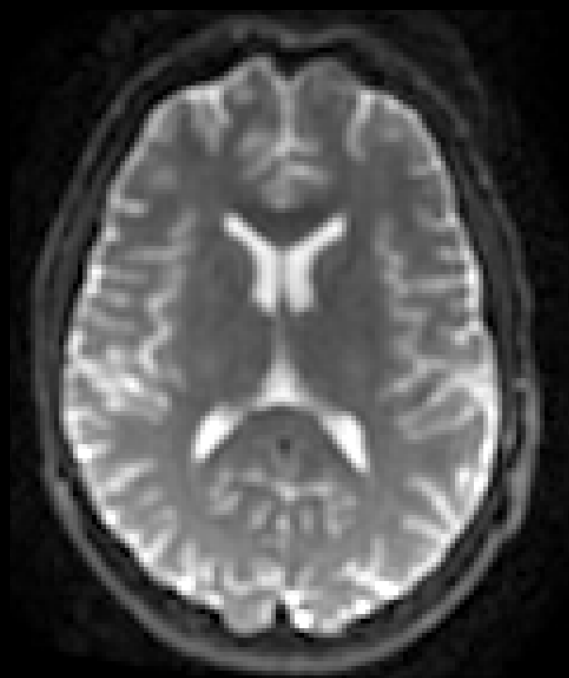
# The Diffusion Tensor



$$\underline{\underline{D}} = \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{bmatrix}$$

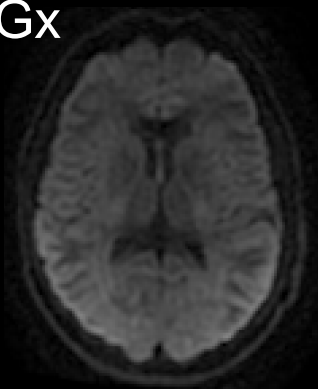
Basser, P, *et. al.* J Magn Reson B (1994) 3 : 247-254

# DTI



$b = 0 \text{ s/mm}^2$

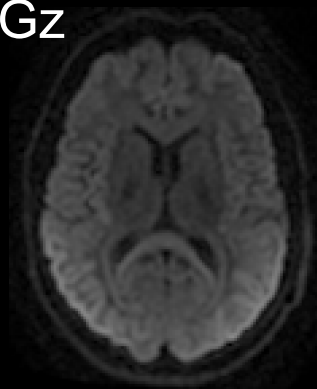
Gx



Gy



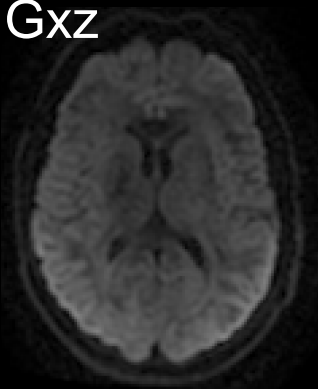
Gz



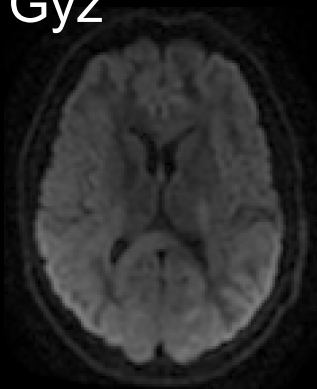
Gxy



Gxz

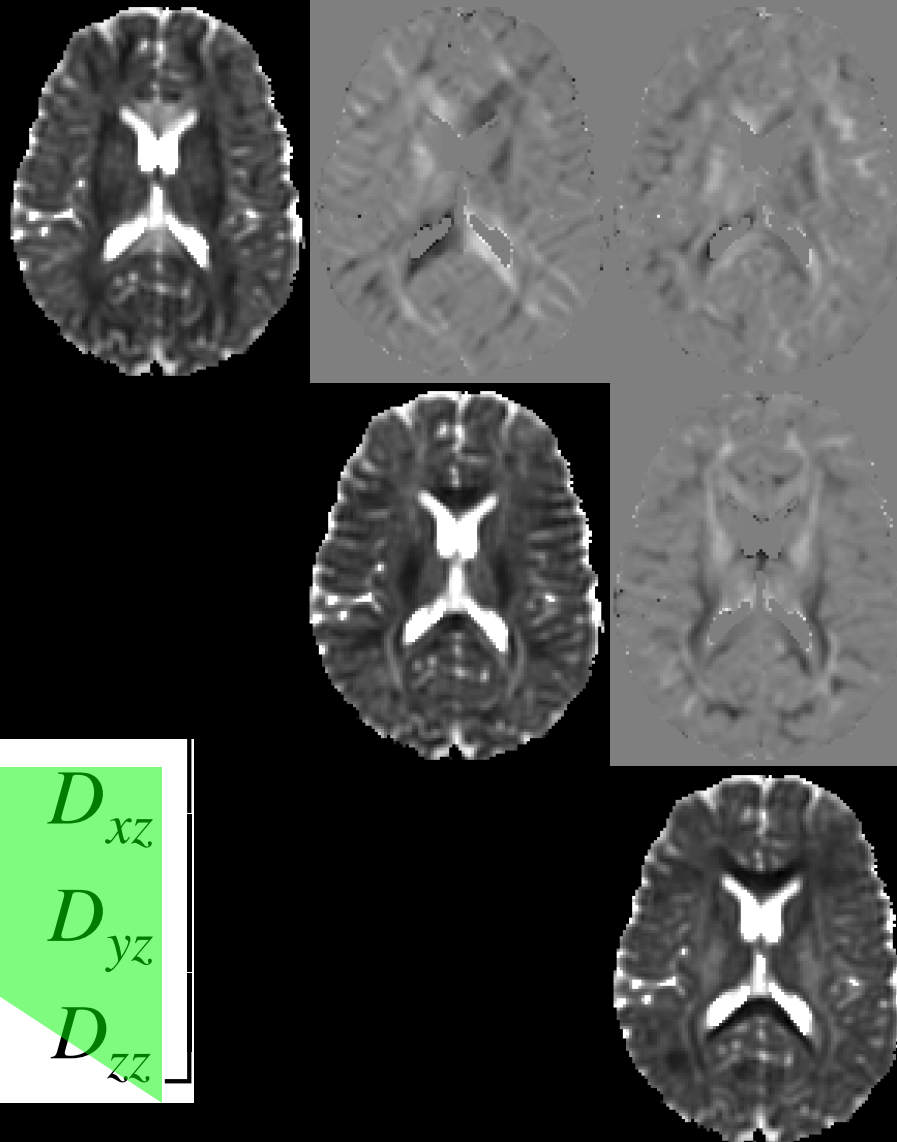


Gyz



$b = 1100 \text{ s/mm}^2$

# Calculate Diffusion Tensor

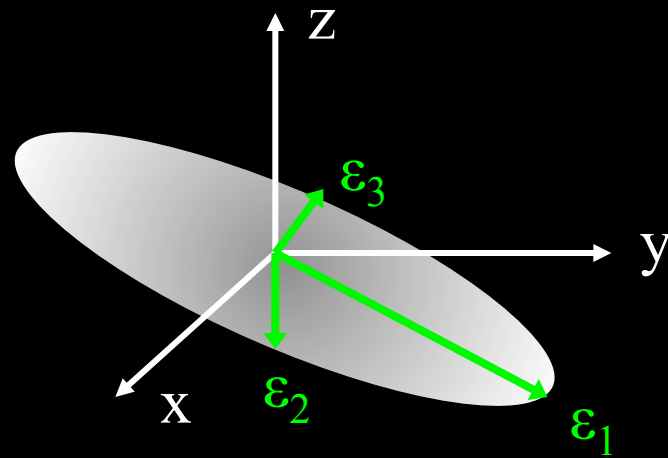


$$\underline{\underline{D}} = \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{bmatrix}$$

# Diagonalize DT

$$\underline{\underline{D}} = \begin{bmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{bmatrix}$$

Eigenvalues



Eigenvectors

# Quantitative Parameters

$$\underline{D} = \begin{bmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{bmatrix}$$

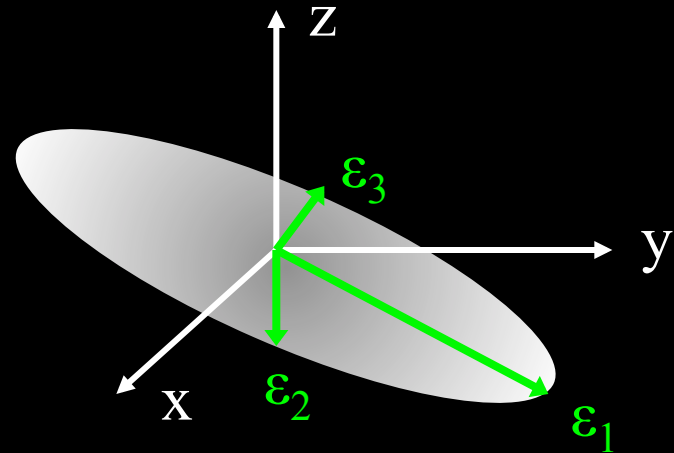
**Average Diffusivity**

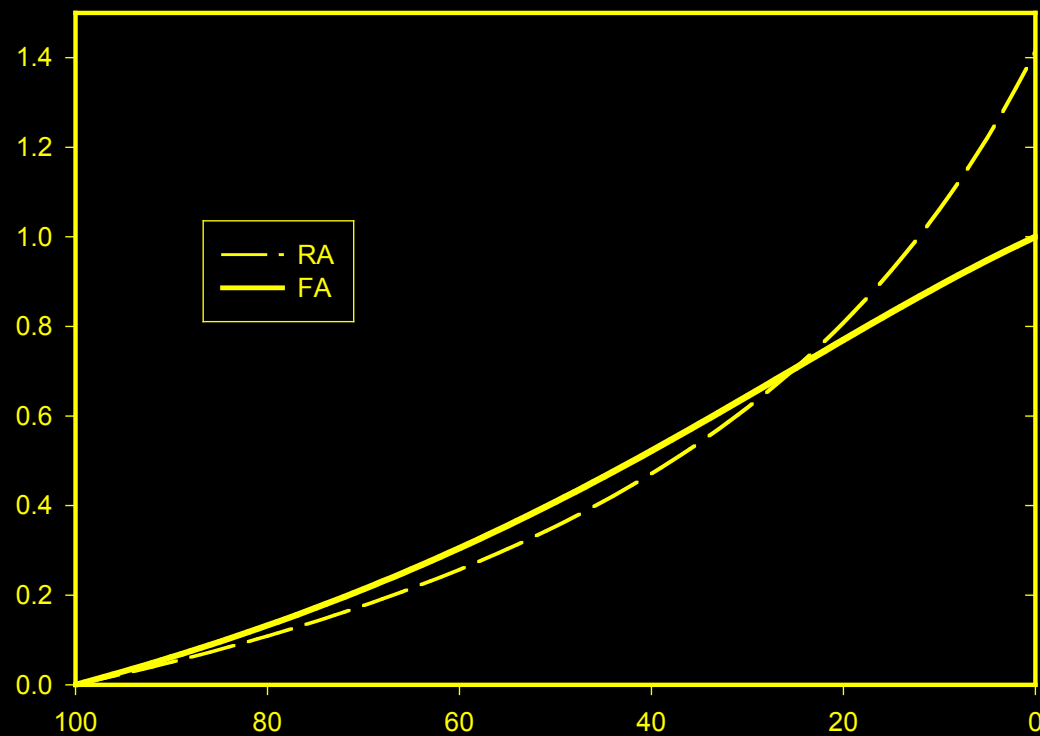
$$\langle D \rangle = \frac{\lambda_1 + \lambda_2 + \lambda_3}{3}$$

**Fractional Anisotropy**

$$FA = \frac{\sqrt{3(\lambda_1 - \langle \lambda \rangle)^2 + (\lambda_2 - \langle \lambda \rangle)^2 + (\lambda_3 - \langle \lambda \rangle)^2}}{\sqrt{2(\lambda_1^2 + \lambda_2^2 + \lambda_3^2)}}$$

$$0 \leq FA \leq 1$$





isotropic



anisotropic

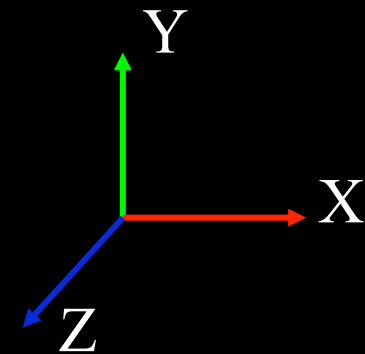
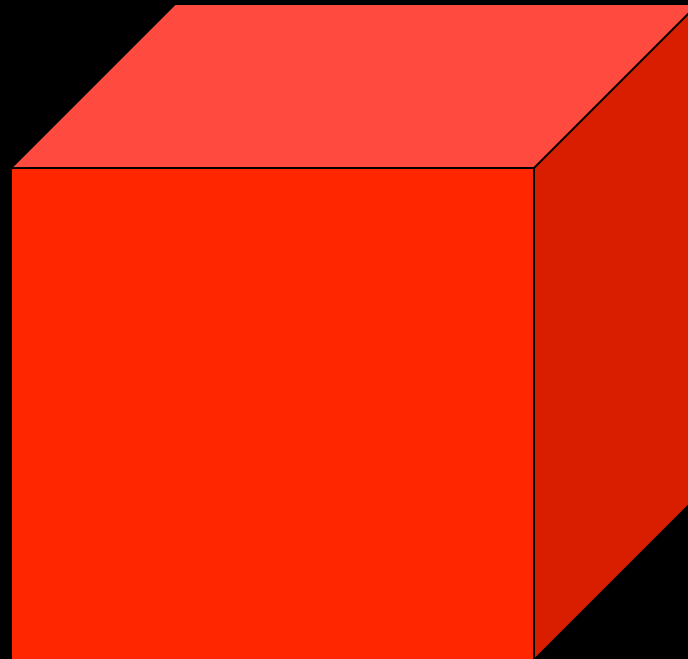
$\langle D \rangle$



FA



# Directional Encoding for DTI

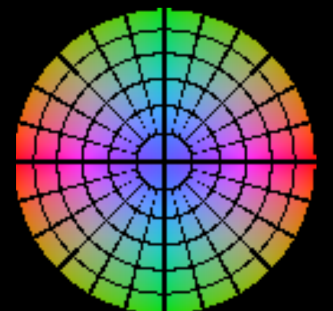
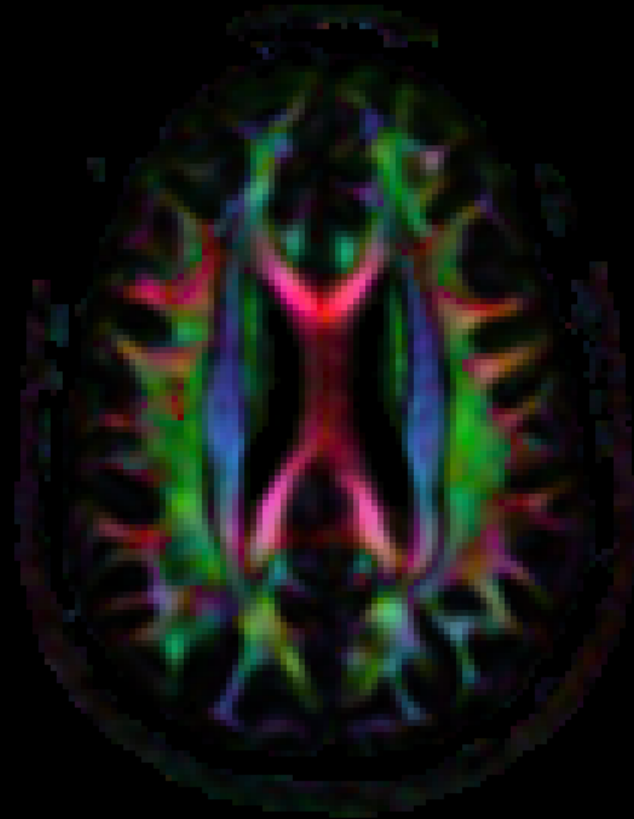


$$\underline{D} = \begin{bmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{bmatrix}$$

Pajevic S. and Pierpaoli C., Magn Reson Med (1999) 43 : 526-540

$\langle D \rangle$

Directional Encoded Color Map

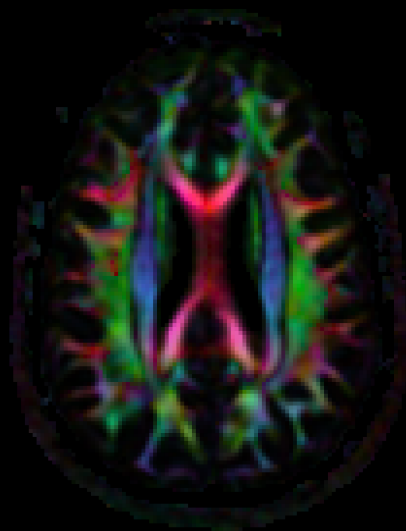




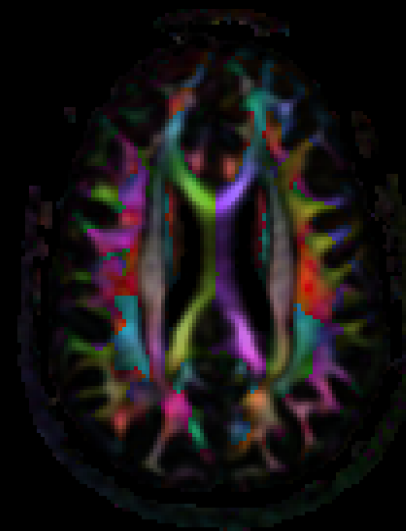
<D>



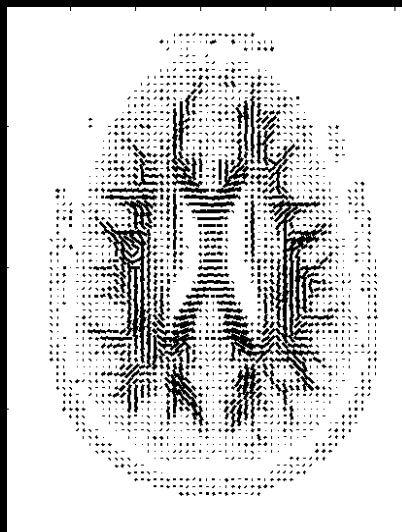
FA



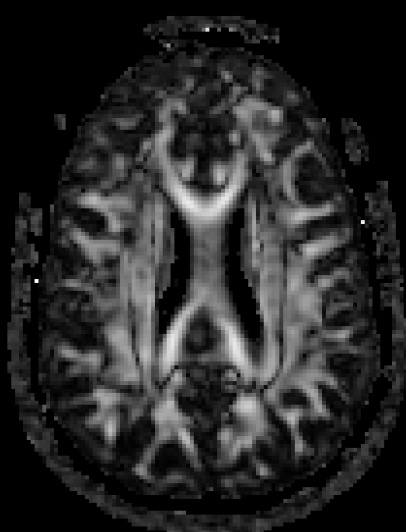
DEC



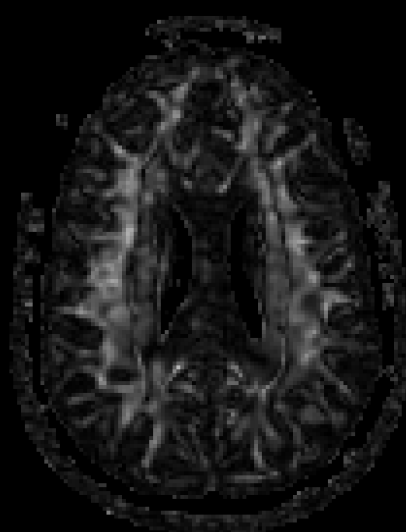
No sym DEC



Line Field



Linear



Planar



Spherical

# Applications of DTI

- Cerebral Ischemia (Stroke)
- Brain Cancer and Effects of Radiotherapy
- Multiple Sclerosis
- Epilepsy
- Metabolic Disorders
- Normal Brain Maturation and Aging
- Traumatic Brain Injury
- Alzheimer's Disease
- Amyotrophic Lateral Sclerosis
- Niemann-Pick type C Disease
- Dementias
- Connectivity

# Outline

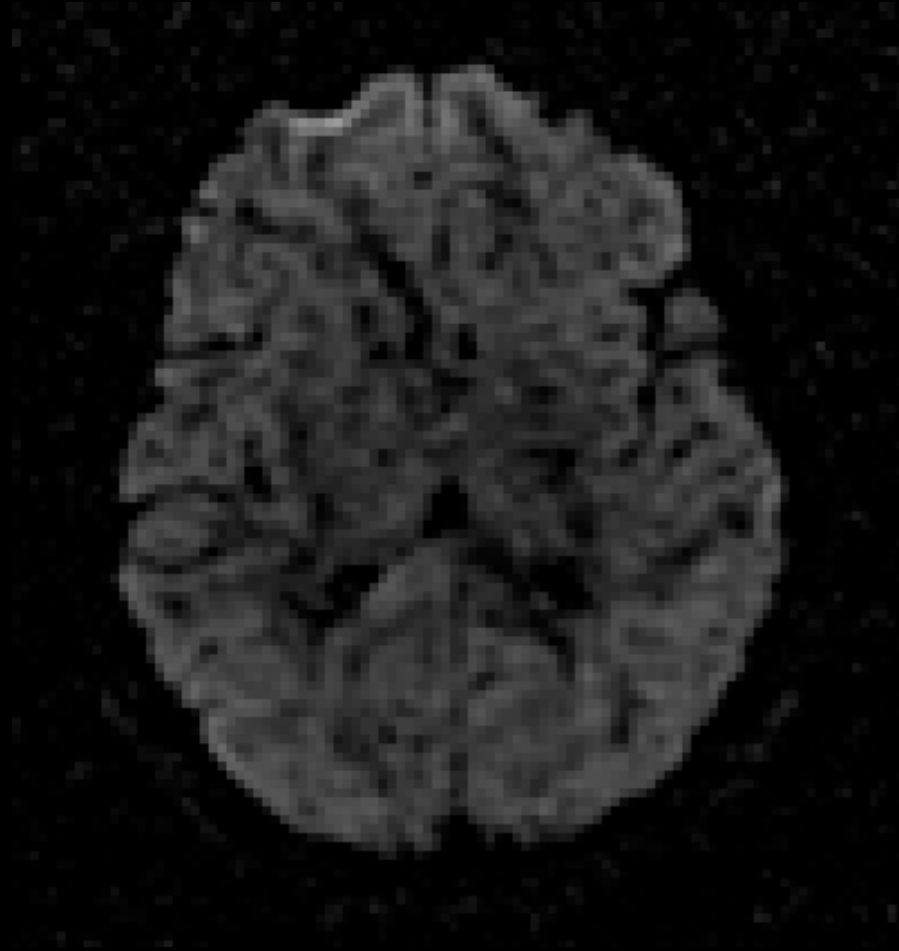
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# Typical DW SSEPI

## PRO

Insensitive to  
Bulk motion

Time Efficient



## CON

Low Resolution

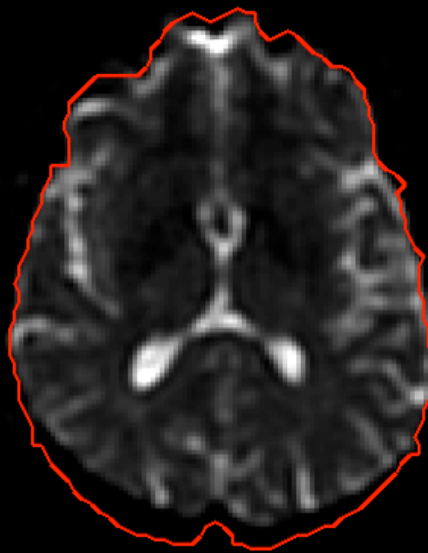
Distortions - Field  
inhomogeneities

Distortions -  
Diffusion weighting

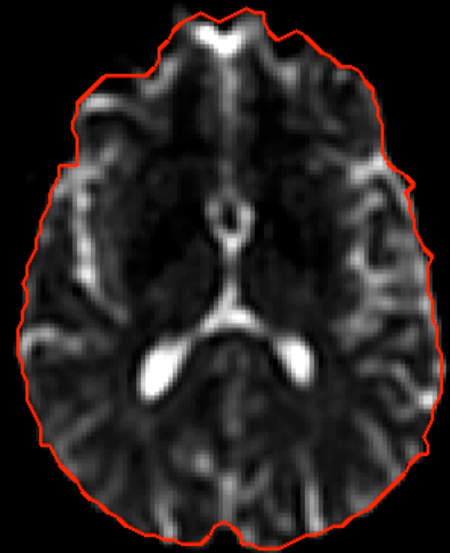
# CON: Distortions from field inhomogeneities



T2-weighted  
FSE

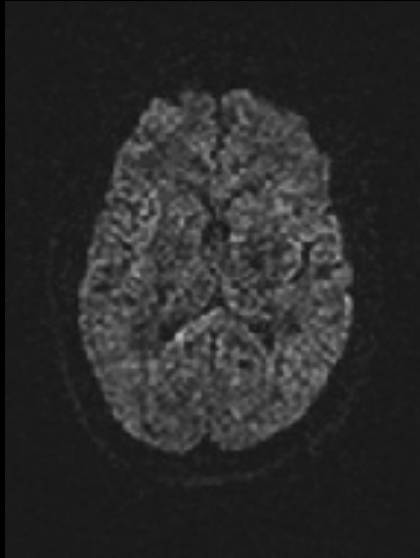


Non-diffusion-weighted  
SSEPI

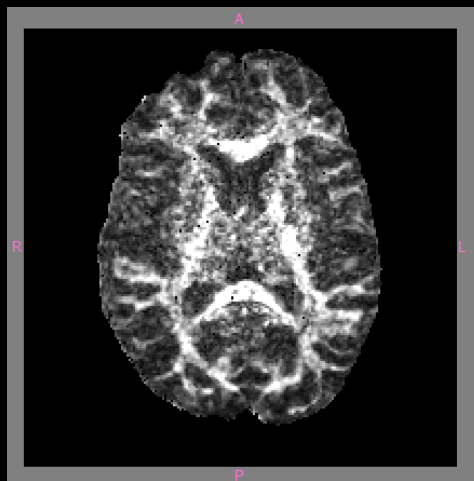
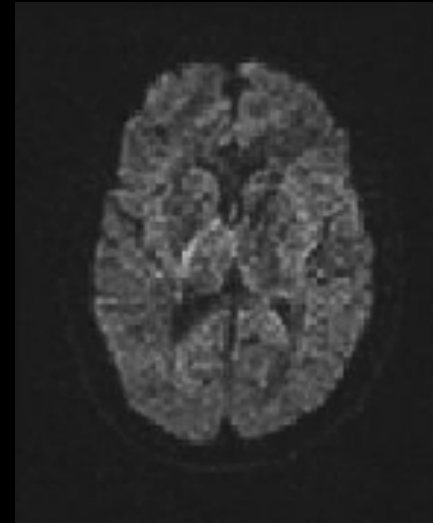


SSEPI  
corrected

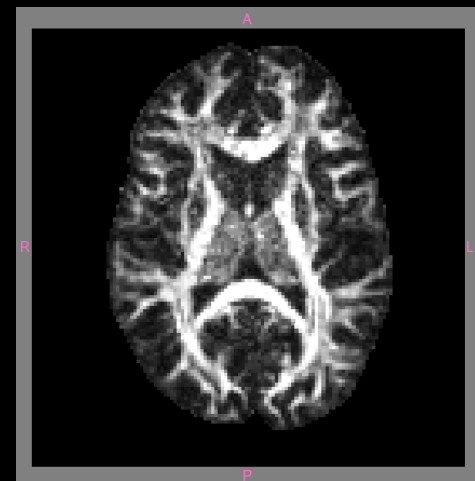
# CON: Distortions from DW



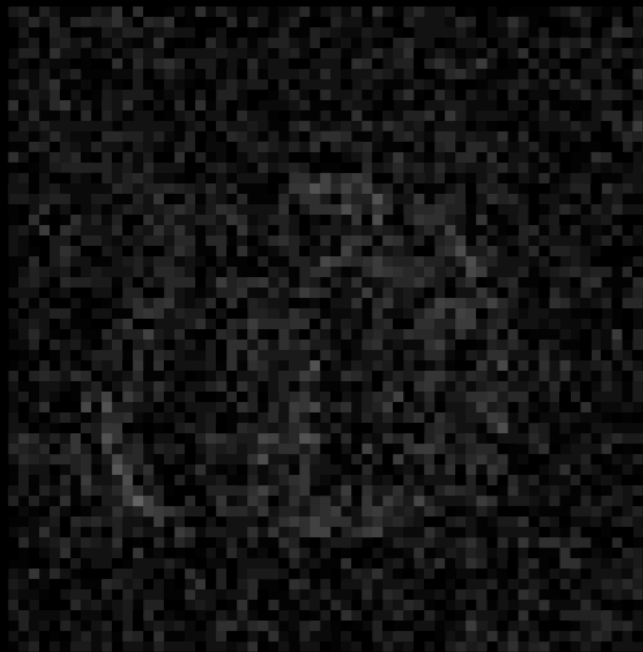
DW  
SSEPI  
volumes



FA maps



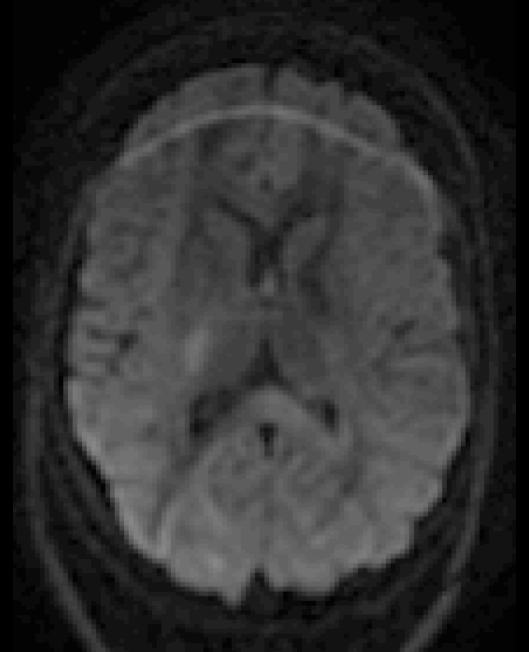
# Other Artifacts



Large Motion



Cardiac Pulsation



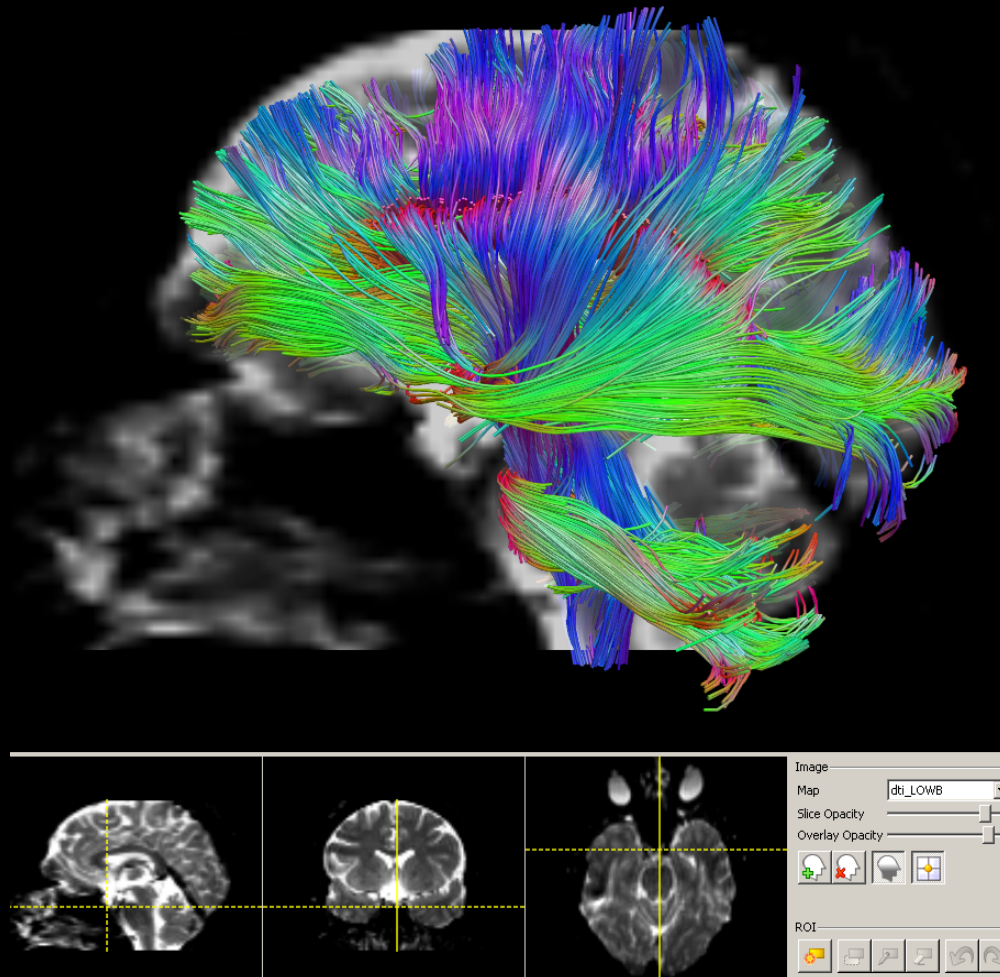
Fat  
(Shifted Image)

# Outline

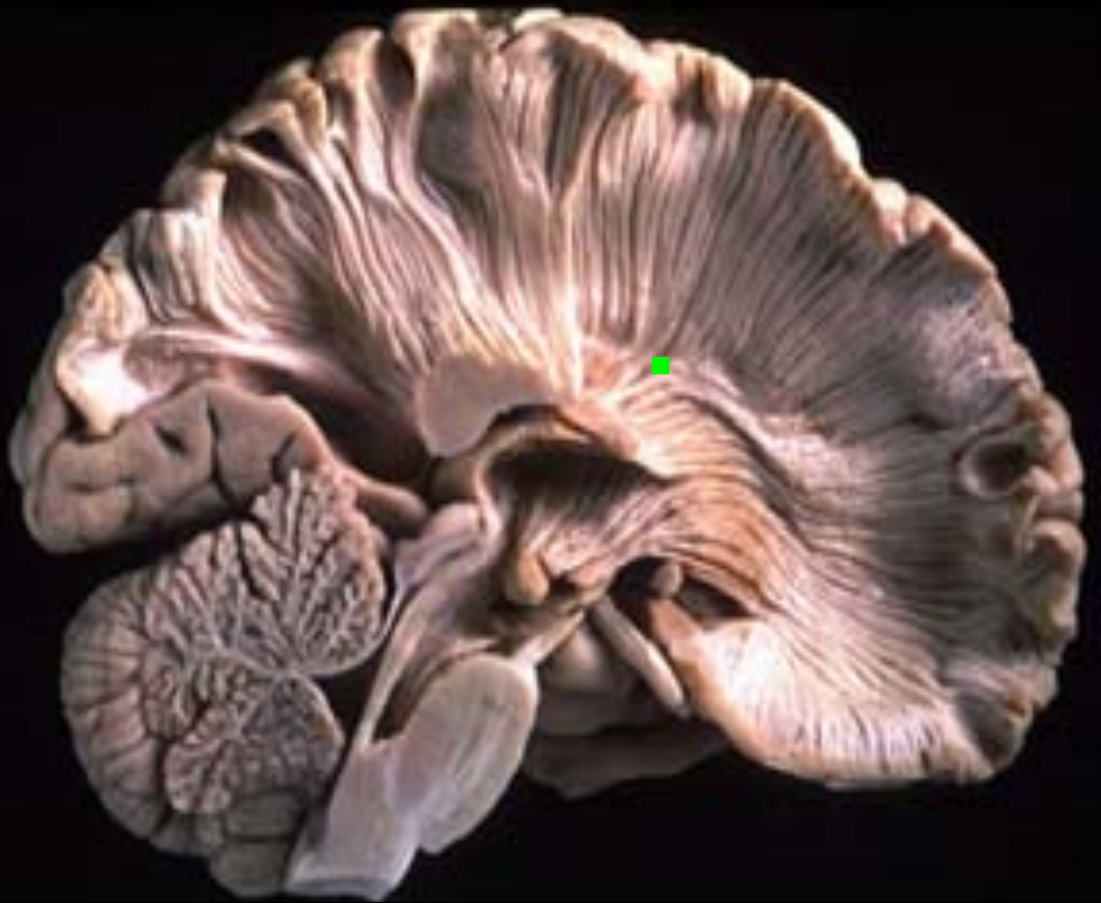
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# What is Tractography?

The use of orientation information from diffusion imaging to reconstruct estimates of white matter pathways in the brain.



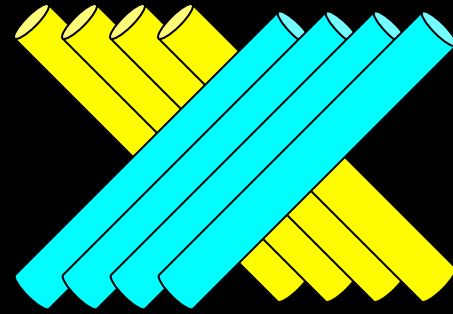
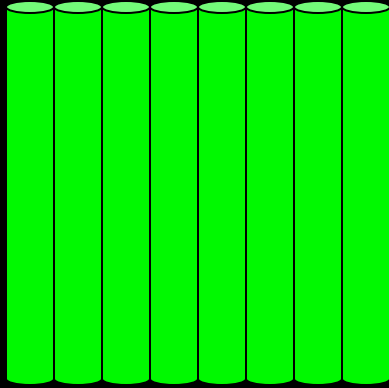
# Limitation to DTI comes from partial volume effects



Typical resolution  
for SSEPI DTI  
 $2.5 \times 2.5 \times 2.5$  mm

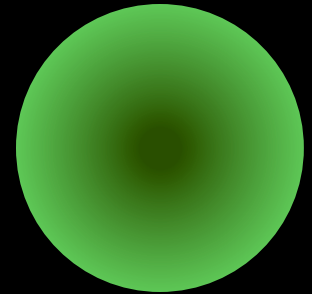
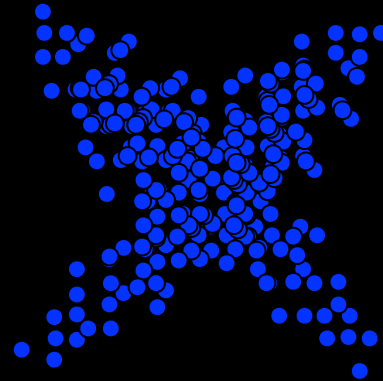
Cortical projection systems of left cerebral hemisphere

# Partial Volume Effect



distribution

DT ellipsoid



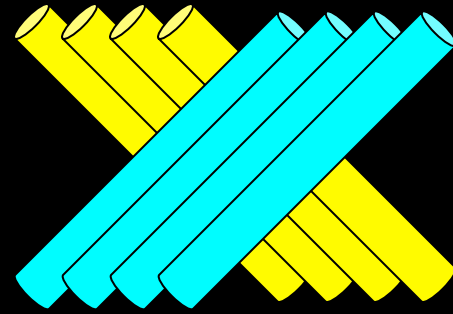
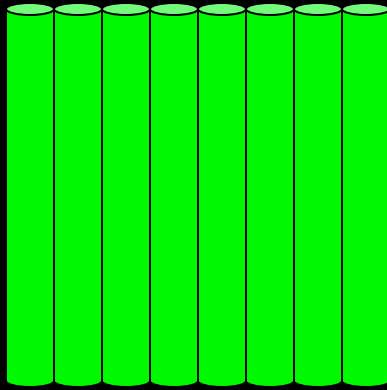
distribution

DT ellipsoid

# Beyond Standard DTI

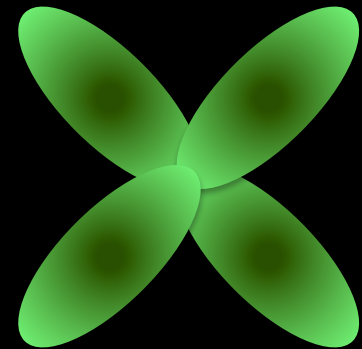
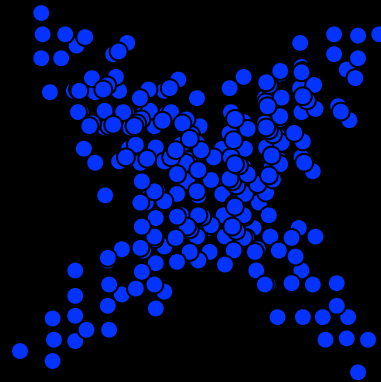
- High Angular Resolution Diffusion Imaging (HARDI)
  - Multi-tensor models
  - Non-parametric algorithms
    - DSI, Qball, SD, PAS

# Non-parametric Algorithms



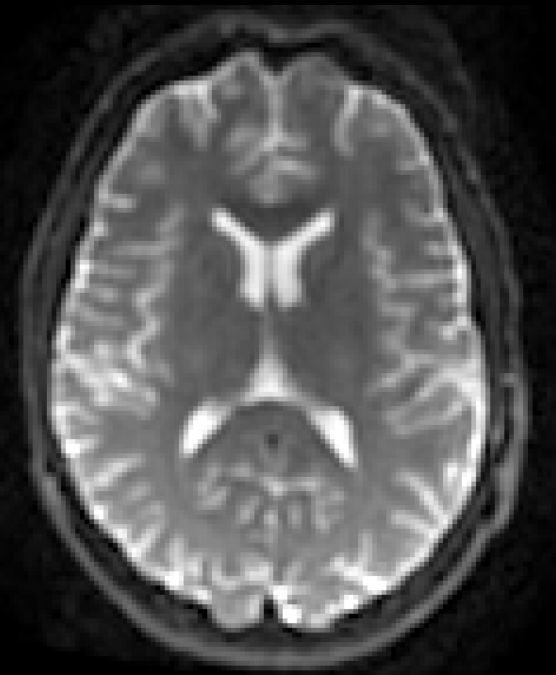
distribution

fODF

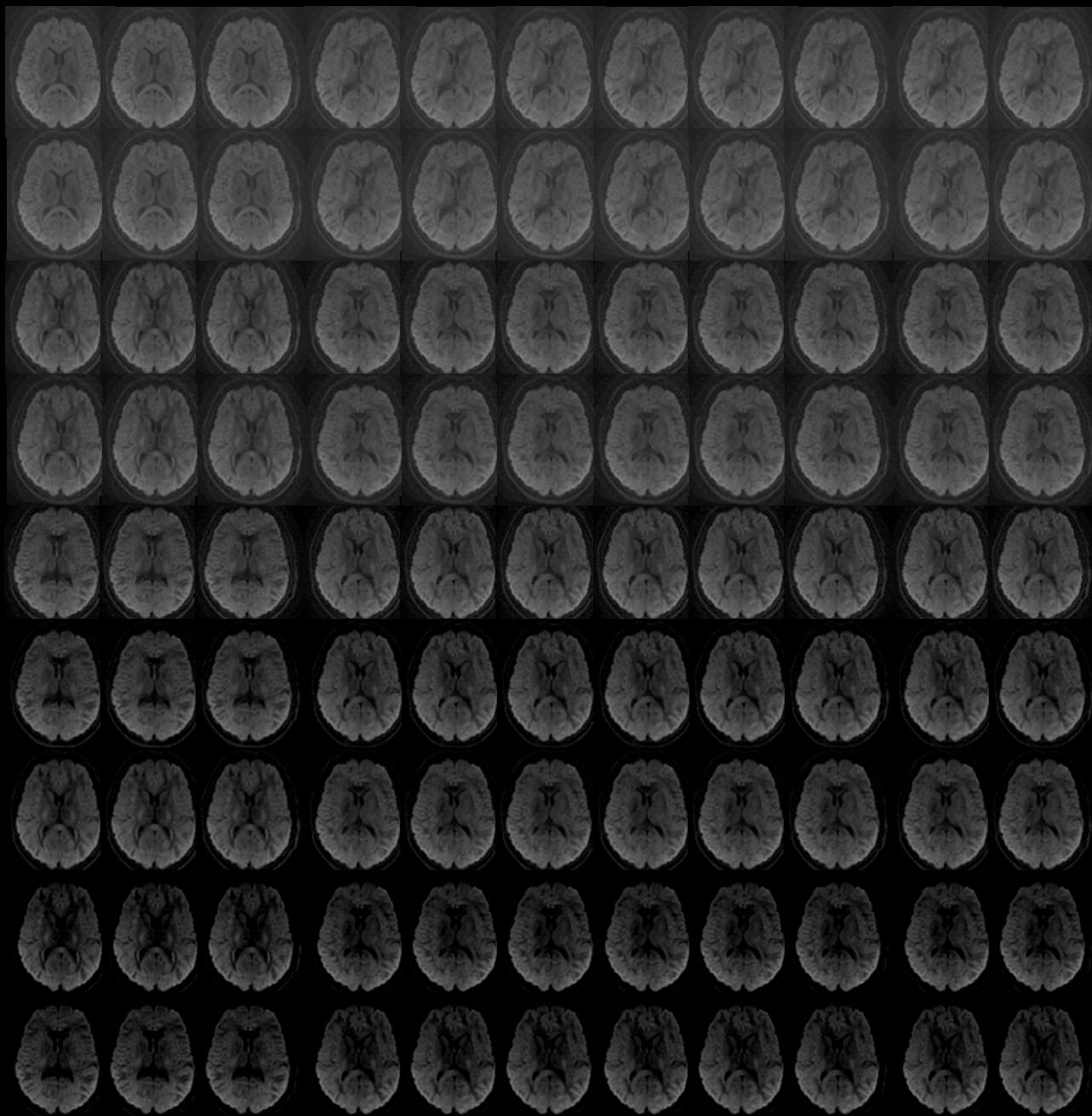


distribution

fODF



$b = 0 \text{ s/mm}^2$



# ACKNOWLEDGEMENTS

Peter Bandettini, PhD

Carlo Pierpaoli, MD, PhD

Ted Trouard, PhD

Lindsay Walker, MS

Kathy Warren, MD

Emilie Steffen

Dan Handwerker, PhD

THANK YOU